PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

United States Patent and Trademark Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 03 November 1998 (03.11.98)	
International application No. PCT/CA98/00325	**Applicant's or agent's file reference** 7841-68
International filing date (day/month/year) 07 April 1998 (07.04.98)	**Priority date** (day/month/year) 07 April 1997 (07.04.97)
Applicant PRICE, Hugh, W. et al	

1. The designated Office is hereby notified of its election made:

   [X] in the demand filed with the International Preliminary Examining Authority on:

   13 October 1998 (13.10.98)

   [ ] in a notice effecting later election filed with the International Bureau on:

   _____

2. The election [X] was

   [ ] was not

   made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer F. Baechler
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

Form PCT/IB/331 (July 1992)

2315968

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
7841-68		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/CA 98/ 00325	07/04/1998	07/04/1997
Applicant		
CANGENE CORPORATION et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. [X] **Certain claims were found unsearchable** (see Box I).

2. [ ] **Unity of invention is lacking** (see Box II).

3. [ ] The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing
   - [ ] filed with the international application.
   - [ ] furnished by the applicant separately from the international application,
     - [ ] but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
   - [ ] Transcribed by this Authority

4. With regard to the **title,**
   - [ ] the text is approved as submitted by the applicant
   - [X] the text has been established by this Authority to read as follows:

INTRAVENOUS IMMUNE GLOBULIN FORMULATION CONTAINING A NON-IONIC SURFACE ACTIVE AGENT WITH IMPROVED PHARMACOKINETIC PROPERTIES

5. With regard to the **abstract,**
   - [X] the text is approved as submitted by the applicant
   - [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is:
   Figure No. 2
   - [X] as suggested by the applicant.
   - [ ] because the applicant failed to suggest a figure.
   - [ ] because this figure better characterizes the invention.
   - [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 98/ 00325

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claims 18-21 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 98/00325

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K39/395

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 278 422 A (GREEN CROSS CORPORATION) 17 August 1988 see the whole document ---	1-21
A	WO 95 01155 A (UNILEVER PLC) 12 January 1995 see the whole document ---	1-21
A	EP 0 764 447 A (BAYER CORPORATION PITTSBURGH) 26 March 1997 see the whole document ---	1-21
A	CA 2 151 409 A (PURISSIMUS) 6 November 1996 see the whole document ---	1-21

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
24 November 1998	08/12/1998

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Moreau, J

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Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 98/00325

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	KALEVI J.A. ET AL.: "Modulation of antibody kinetics by the cell membrane active agent tween 80 in vivo" ANTICANCER RESEARCH, vol. 16, no. 6b, 1996, pages 3542-3550, XP002085447 see the whole document	1-21
A	EP 0 318 081 A (AKZO N.V.) 31 May 1989 cited in the application see the whole document	1-21
A	EP 0 073 371 A (CUTTER LABORATORIES INC.) 9 March 1983 cited in the application see the whole document	1-21

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/CA 98/00325

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 278422 A	17-08-1988	JP 2547556 B	23-10-1996
		JP 63192724 A	10-08-1988
		CA 1331135 A	02-08-1994
		DE 3889938 D	14-07-1994
		DE 3889938 T	03-11-1994
		ES 2052615 T	16-07-1994
		KR 9608653 B	28-06-1996
		US 4876088 A	24-10-1989
WO 9501155 A	12-01-1995	AU 7345094 A	24-01-1995
EP 764447 A	26-03-1997	AU 6569096 A	27-03-1997
		JP 9124507 A	13-05-1997
CA 2151409 A	06-11-1900	NONE	
EP 318081 A	31-05-1989	AU 2579188 A	01-06-1989
		CA 1317899 A	18-05-1993
		DK 648088 A	28-05-1989
		ES 2051830 T	01-07-1994
		GR 3002971 T	25-01-1993
		IE 60719 B	10-08-1994
		JP 1168624 A	04-07-1989
		MX 165991 B	14-12-1992
		US 4902500 A	20-02-1990
EP 73371 A	09-03-1900	US 4396608 A	02-08-1983
		AT 16567 T	15-12-1985
		AU 549204 B	16-01-1986
		AU 8726582 A	03-03-1983
		CA 1183084 A	26-02-1985
		JP 2020314 C	19-02-1996
		JP 6094421 B	24-11-1994
		JP 58043914 A	14-03-1983
		JP 5208918 A	20-08-1993
		JP 7061956 B	05-07-1995
		US 4499073 A	12-02-1985

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61K 39/395

A2

(11) International Publication Number: **WO 98/44948**

(43) International Publication Date: 15 October 1998 (15.10.98)

(21) International Application Number: PCT/CA98/00325

(22) International Filing Date: 7 April 1998 (07.04.98)

(30) Priority Data:
60/041,921 7 April 1997 (07.04.97) US

(71) Applicant *(for all designated States except US)*: CANGENE CORPORATION [CA/CA]; 104 Chancellor Metheson Road, Winnipeg, Manitoba R3T 2N2 (CA).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: PRICE, Hugh, W. [CA/CA]; 350 Kingston Crescent, Winnipeg, Manitoba R2M 0T8 (CA). WOLOSKI, B., Michael, R. [CA/CA]; Cangene Corporation, 104 Chancellor Matheson, Winnipeg, Manitoba R3T 2N2 (CA).

(74) Agent: BERESKIN & PARR; 40th floor, 40 King Street West, Toronto, Ontario M5H 3Y2 (CA).

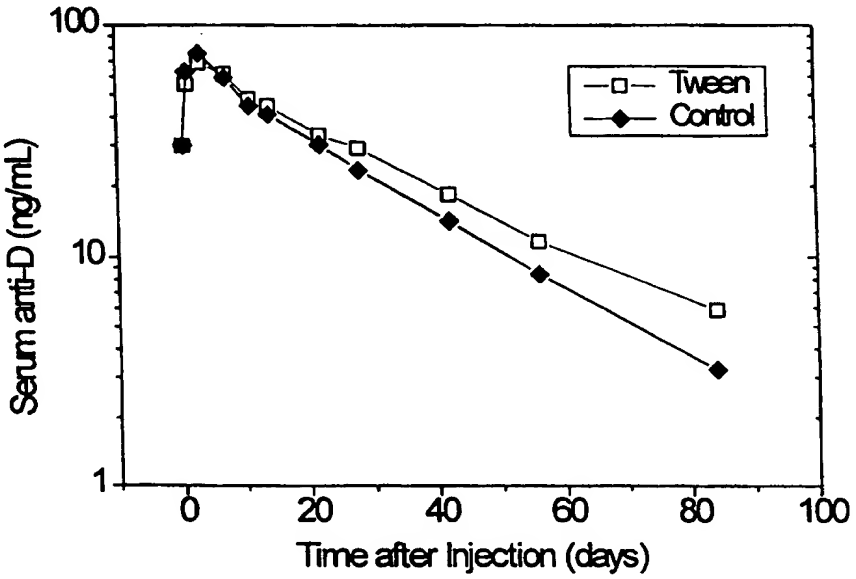
(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
Without international search report and to be republished upon receipt of that report.

(54) Title: INTRAVENOUS IMMUNE GLOBULIN FORMULATION CONTAINING A NON-IONIC SURFACE ACTIVE AGENT WITH IMPROVED PHARMACOKINETIC PROPERTIES

(57) Abstract

Addition of a non-ionic surface active agent to an immune globulin formulation extends the serum half-life of relatively pure and non-aggregated immune globulin suitable for intravenous injectionor infusion. The non-ionic surface active agent may be a sorbitan ester or a polyoxyethylene sorbitan ester of a fatty acid. Formulations of the present invention is therapeutically advantageous over conventional formulations in that an extended serum half-life of the immune globulin improves its therapeutic effectiveness, reduces the frequency of drug administration and/or lowers the therapeutic effective dosage required and cost of treatment.



FOR THE PURPOSES OF INFORMATION ONLY

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PATENT COOPERATION TREATY

PCT

REC'D 04 AUG 1999
WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
7841-68		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA98/00325	07/04/1998	07/04/1997
International Patent Classification (IPC) or national classification and IPC		
A61K39/395		
Applicant		
CANGENE CORPORATION et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 4 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
13/10/1998	30.07.99
Name and mailing address of the international preliminary examining authority:	Authorized officer
European Patent Office D-80298 Munich Tel. (+49-89) 2399-0 Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Tilkorn, A-C Telephone No. (+49-89) 2399 8688

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA98/00325

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-28 as originally filed

Claims, No.:

1-26 as received on 22/06/1999 with letter of 15/06/1999

Drawings, sheets:

1/2,2/2 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

see separate sheet

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 18-22.

because:

☒ the said international application, or the said claims Nos. 18-22 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-16,18-26
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-16,18-26
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-16,23-26
	No:	Claims	

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Section I:

The amendment, namely the introduction of **claim 17**, does not meet the requirements of Art 34 PCT. The non-ionic surfactants glyceryl monooleate and polyvinyl alcohol cannot be found in the application as originally filed. Thus, there is no basis in the original application. Thus, claim 17 is not taken into account in this Report.

Section III:

For the assessment of the present **claims 18-22** on the question whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Section V:

The following documents are referred to in this communication:

D1: EP-A-278 422
D2: WO 95 01155

D1 describes γ- globulin injectable solutions. It makes use of sorbitol in order to stabilize the solution and to prevent the increase of γ- globulin polymer either during preservation or upon administration to a living body (abstract, page 2 line 12-14). The aqueous γ- globulin solution also contains polyethylene glycol and low amounts of NaCl (page 3 line 26-30). The ionic strength is adjusted to 0.0001- 0,1 M (page 3 line 45). It is found in D1 that the stability of γ- globulin increases with the sorbitol concentration (page 9 line 56). In example 5 a γ- globulin concentration of 5% (w/v) is applied and a sorbitol concentration of 5 % (w/v) resulting in a polymer content of 0,00 % (w/v) (page 10 line 2-7).

D2 discloses oral compositions comprising an antibody and a non-ionic surfactant

as stabilizer (page 1 line 31-35; Claim 6). Examples for non-ionic surfactants given are polyoxyethylene sorbitan monolaurate and polyoxyethylene sorbitan monooleate and mixtures thereof (page 3 line 13-17). The suitable non-ionic surfactant concentrations range from 0,01-6% (w/w)(page 3 line 19-21) or 0,02-10% (w/v) (page 10 line 10-12). Another suitable ingredient of the composition is glycine (page 13 table 5).

1. **Claim 1** meets the requirements of Art 33(2)PCT, because in none of the available documents an immune globulin preparation for intravenous injection containing at least one non-ionic surface active agent is disclosed.

2. D1 that is considered to represent the closest prior art, discloses injectable solutions of γ- globulin containing sorbitol as a stabilizer and having a low electrical conductivity.
The problem to be solved over D1 can be regarded as how to provide an alternative immune globulin preparation with an increased serum half-life.
The use of non ionic surfactants such as sorbitan esters is described for oral compositions (D2) in order to improve the compatibility with the antibody, to provide improved immunoreactivity on longer term storage and to enhance antibody binding (D2: page 1 line 35- page 2 line 2). A skilled person would not expect a longer serum half-life of the antibodies due to non-ionic surfactant in the immune globulin preparation. Thus, claim 1 appears to be inventive according to Article 33 (3) PCT.
As the independent claim appears to be new and inventive, the dependent claims 2-15 which relate to more specific embodiments also seem to fulfil the requirements of Article 33 (2),(3) PCT.

   Claim 16 relates to a γ- globulin preparation containing Polysorbate 80™, that is a non ionic surfactant and a sorbitan ester (polyoxyethylene sorbitan monooleate). Thus, claim 16 appears to be new and inventive (Article 33(2),(3) PCT).

3. **Claim 23** relates to an immune globulin preparation comprising an immune globulin with a purity of greater than about 95% and a monomeric protein content of greater than about 94% and at least one non-ionic surface active agent.
Only high-purity preparations can be used for intravenous administration

(application: page 3 line 5-8). As mentioned above, known preparation suitable for intravenous administration do not contain non-ionic surfactants. Thus, claim 23 meets the requirements of Articles 33(2) and (3) PCT. The same applies to the dependent **claims 24-26** (see Section VIII (2) hereinbelow).

4. **Claims 18-22** relate to the medical use of the immune globulin preparations containing non-ionic surfactant and are considered to meet the requirements of Art 33 (2 and 3) PCT, because in none of the available documents such preparations are used to increase the serum half-life of the antibodies or to reduce the elevation of neutrophils.

Section VII:

- To meet the requirements of Rule 5.1 a) PCT, the document D1 and D2 should have been identified in the description and the relevant background art disclosed therein should have been briefly discussed.

- Application numbers should have been replaced by the corresponding publication numbers (e.g. page 6 line 7).

- The sentences on page 13 line 30-33 and on page 28 line 14-20 should have been deleted.

Section VIII:

1. The wording of **claim 1** should have been corrected by replacing "...hyperimmune...." by "...immune...", as a protein cannot be a hyperimmune gobulin.

2. **Claims 24-26** do not meet the requirements of Art 6 PCT, because their category is not clear. On one hand they refer to a preparation, but on the other hand they are dependent on claim 22 which is a method claim.
For the assessment of industrial applicability, it has been assumed that a typing error has occurred and that the dependency of claims 24 and 25 is meant to refer to claim 23 instead of claim 22.

We Claim:

1. An immune globulin preparation for intravenous injection comprising a hyperimmune globulin and at least one non-ionic surface active agent, said one or more non-ionic surface active agent(s) in a concentration sufficient to increase the serum half-life of the immune globulin.

2. The preparation according to claim 1 wherein the immune globulin is anti-Rh_oD immune globulin.

3. The preparation according to claim 2 wherein the anti-Rh_oD immune globulin has an IgG purity of greater than about 95% and a monomeric protein content of greater than about 94%.

4. The preparation according to claim 3 which is aqueous.

5. The preparation according to claim 1 wherein the immune globulin is anti-c immune globulin.

6. The preparation according to claim 5 wherein the anti-c immune globulin has an IgG purity of greater than about 95% and a monomeric protein content of greater than about 94%.

7. The preparation according to claim 6 which is aqueous.

8. The preparation according to claim 1 wherein the concentration of the immune globulin is about 2 weight percent to about 10 weight percent.

9. The preparation according to claim 1 wherein the one or more non-ionic surface active agent(s) is(are) a sorbitan ester of a fatty acid.

10. The preparation according to claim 9 wherein the non-ionic surface active agent(s) is(are) selected from the group consisting of sorbitan monolaurate, sorbitan monopalmitate, sorbitan monostearate, sorbitan tristearate, sorbitan monooleate, and sorbitan trioleate.

11. The preparation according to claim 1 wherein the one or more non-ionic surface active agent(s) is(are) a polyoxyethylene sorbitan ester of a fatty acid.

12. The preparation according to claim 11 wherein the non-ionic surface active agent(s) is(are) selected from the group consisting of polyoxyethylene (20) sorbitan monolaurate, polyoxyethylene (4) sorbitan monolaurate, polyoxyethylene (20) sorbitan monopalmitate, polyoxyethylene (20) sorbitan monostearate, polyoxyethylene (4) sorbitan monostearate, polyoxyethylene (20) sorbitan tristearate, polyoxyethylene (20) sorbitan monooleate, polyoxyethylene (5) sorbitan monooleate, and polyoxyethylene (20) sorbitan trioleate.

13. The preparation according to claim 1 wherein two or more non-ionic surface active agents are selected from the group consisting of polyoxyethylene (20) sorbitan monolaurate, polyoxyethylene (4) sorbitan monolaurate, polyoxyethylene (20) sorbitan monopalmitate; polyoxyethylene (20) sorbitan monostearate, polyoxyethylene (4) sorbitan monostearate, polyoxyethylene (20) sorbitan tristearate, polyoxyethylene (20) sorbitan monooleate, polyoxyethylene (5) sorbitan monooleate, and polyoxyethylene (20) sorbitan trioleate, sorbitan monolaurate, sorbitan monopalmitate, sorbitan monostearate, sorbitan tristearate, sorbitan monooleate, and sorbitan trioleate.

14. The preparation according to claim 1 wherein the concentration of the one or more non-ionic surface active agent(s) is(are) about 0.01 weight percent to about 0.5 weight percent.

15. The preparation according to claim 1 wherein the immune globulin preparation is a lyophilized preparation.

16. An aqueous or a lyophilized immune globulin preparation wherein the immune globulin has an increased serum half-life comprising:

about 3-8% human anti-Rh_oD immune globulin with an IgG purity of greater than 95% and a monomeric protein content of greater than 94%;

sodium chloride at about 0.25% (w/v);

very low level buffer with essentially no ionic strength;

Polysorbate 80® at about 0.01% to about 0.5% (w/v); and

L-glycine at about 0.1M.

17. The preparation according to claim 1 wherein the one or more non-ionic surface agents are selected from the group consisting of glyceryl monooleate; and a polyvinyl alcohol.

18. A use of an immune globulin preparation according to any one of claims 1 to 17 to increase the serum half-life of an immune globulin.

19. A use of an immune globulin preparation according to any one of claims 1 to 17 to reduce the elevation of neutrophil counts..

20. A method of increasing the serum half-life of an immune globulin comprising administering an immune globulin preparation according to claims 1 to 17 to an animal in need thereof.

21. A method of reducing the elevation of neutrophil counts in a recipient of immune globulin comprising administering an immune globulin preparation according to claims 1 to 17 to an animal in

need thereof.

22. A method according to claim 20 or 21 wherein said immune globulin preparation is administered intravenously.

23. An immune globulin preparation comprising an immune globulin, having a purity of greater than about 95 percent and a monomeric protein content of greater than about 94 percent, and at least one non-ionic surface active agent, said one or more non-ionic surface active agent(s) in a concentration sufficient to increase the serum half life of the immune globulin.

24. The preparation according to claim 22 wherein the immune globulin is anti-Rh_OD immune globulin.

25. The preparation according to claim 22 wherein the immune globulin is anti-c immune globulin.

26. The preparation according to any one of claims 23-25 which is aqueous.

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AMENDED CLAIMS

[received by the International Bureau on 8 February 1999 (08.02.99);
original claims 17-21 replaced by amended claims 18-22;
remaining claims unchanged (4 pages)]

1. An immune globulin preparation comprising an immune globulin and at least one non-ionic surface active agent, said one or more non-ionic surface active agent(s) in a concentration sufficient to increase the serum half-life of the immune globulin.

2. The preparation according to claim 1 wherein the immune globulin is anti-Rh_oD immune globulin.

3. The preparation according to claim 2 wherein the anti-Rh_oD immune globulin has an IgG purity of greater than about 95% and a monomeric protein content of greater than about 94%.

4. The preparation according to claim 3 which is aqueous.

5. The preparation according to claim 1 wherein the immune globulin is anti-c immune globulin.

6. The preparation according to claim 5 wherein the anti-c immune globulin has an IgG purity of greater than about 95% and a monomeric protein content of greater than about 94%.

7. The preparation according to claim 6 which is aqueous.

8. The preparation according to claim 1 wherein the concentration of the immune globulin is about 2 weight percent to about 10 weight percent.

9. The preparation according to claim 1 wherein the one or more non-ionic surface active agent(s) is(are) a sorbitan ester of a fatty acid.

10. The preparation according to claim 9 wherein the non-ionic surface active agent(s) is(are) selected from the group consisting of sorbitan monolaurate, sorbitan monopalmitate, sorbitan monostearate, sorbitan tristearate, sorbitan monooleate, and sorbitan trioleate.

11. The preparation according to claim 1 wherein the one or more non-ionic surface active agent(s) is(are) a polyoxyethylene sorbitan ester of a fatty acid.

12. The preparation according to claim 11 wherein the non-ionic surface active agent(s) is(are) selected from the group consisting of polyoxyethylene (20) sorbitan monolaurate, polyoxyethylene (4) sorbitan monolaurate, polyoxyethylene (20) sorbitan monopalmitate, polyoxyethylene (20) sorbitan monostearate, polyoxyethylene (4) sorbitan monostearate, polyoxyethylene (20) sorbitan tristearate, polyoxyethylene (20) sorbitan monooleate, polyoxyethylene (5) sorbitan monooleate, and polyoxyethylene (20) sorbitan trioleate.

13. The preparation according to claim 1 wherein two or more non-ionic surface active agents are selected from the group consisting of polyoxyethylene (20) sorbitan monolaurate, polyoxyethylene (4) sorbitan monolaurate, polyoxyethylene (20) sorbitan monopalmitate; polyoxyethylene (20) sorbitan monostearate, polyoxyethylene (4) sorbitan monostearate, polyoxyethylene (20) sorbitan tristearate, polyoxyethylene (20) sorbitan monooleate, polyoxyethylene (5) sorbitan monooleate, and polyoxyethylene (20) sorbitan trioleate, sorbitan monolaurate, sorbitan monopalmitate, sorbitan monostearate, sorbitan tristearate, sorbitan monooleate, and sorbitan trioleate.

14. The preparation according to claim 1 wherein the concentration of the one or more non-ionic surface active agent(s) is(are) about 0.01 weight percent to about 0.5 weight percent.

15. The preparation according to claim 1 wherein the aqueous immune globulin preparation is lyophilized to form a dry powder preparation.

16. An aqueous immune globulin preparation wherein the immune globulin has an increased serum half-life comprising:

about 3-8% human anti-Rh_oD immune globulin with an IgG purity of greater than 95% and a monomeric protein content of greater than 94%;

sodium chloride at about 0.25% (w/v);

very low level buffer with essentially no ionic strength;

Polysorbate 80 at about 0.01% to about 0.5% (w/v); and

L-glycine at about 0.1M.

17. The preparation according to claim 1 wherein the one or more non-ionic surface agents are selected from the group consisting of glyceryl monooleate; and a polyvinyl alcohol.

18. A use of an immune globulin preparation according to any one of claims 1 to 17 to increase the serum half-life of an immune globulin.

19. A use of an immune globulin preparation according to any one of claims 1 to 17 to reduce the elevation of neutrophil counts.

20. A method of increasing the serum half-life of an immune globulin comprising administering an immune globulin preparation according to claims 1 to 17 to an animal in need thereof.

21. A method of reducing the elevation of neutrophil counts in a recipient of immune globulin comprising administering an immune globulin preparation according to claims 1 to 17 to an animal in need thereof.

22. A method according to claim 20 or 21 wherein said immune globulin preparation is administered intravenously.

We Claim:

1. An immune globulin preparation comprising an immune globulin and at least one non-ionic surface active agent, said one or more non-ionic surface active agent(s) in a concentration sufficient to increase the serum half-life of the immune globulin.

2. The preparation according to claim 1 wherein the immune globulin is anti-Rh_oD immune globulin.

3. The preparation according to claim 2 wherein the anti-Rh_oD immune globulin has an IgG purity of greater than about 95% and a monomeric protein content of greater than about 94%.

4. The preparation according to claim 3 which is aqueous.

5. The preparation according to claim 1 wherein the immune globulin is anti-c immune globulin.

6. The preparation according to claim 5 wherein the anti-c immune globulin has an IgG purity of greater than about 95% and a monomeric protein content of greater than about 94%.

7. The preparation according to claim 6 which is aqueous.

8. The preparation according to claim 1 wherein the concentration of the immune globulin is about 2 weight percent to about 10 weight percent.

9. The preparation according to claim 1 wherein the one or more non-ionic surface active agent(s) is(are) a sorbitan ester of a fatty acid.

10. The preparation according to claim 9 wherein the non-ionic surface active agent(s) is(are) selected from the group consisting of sorbitan monolaurate, sorbitan monopalmitate, sorbitan monostearate, sorbitan tristearate, sorbitan monooleate, and sorbitan trioleate.

11. The preparation according to claim 1 wherein the one or more non-ionic surface active agent(s) is(are) a polyoxyethylene sorbitan ester of a fatty acid.

12. The preparation according to claim 11 wherein the non-ionic surface active agent(s) is(are) selected from the group consisting of polyoxyethylene (20) sorbitan monolaurate, polyoxyethylene (4) sorbitan monolaurate, polyoxyethylene (20) sorbitan monopalmitate, polyoxyethylene (20) sorbitan monostearate, polyoxyethylene (4) sorbitan monostearate, polyoxyethylene (20) sorbitan tristearate, polyoxyethylene (20) sorbitan monooleate, polyoxyethylene (5) sorbitan monooleate, and polyoxyethylene (20) sorbitan trioleate.

13. The preparation according to claim 1 wherein two or more non-ionic surface active agents are selected from the group consisting of polyoxyethylene (20) sorbitan monolaurate, polyoxyethylene (4) sorbitan monolaurate, polyoxyethylene (20) sorbitan monopalmitate; polyoxyethylene (20) sorbitan monostearate, polyoxyethylene (4) sorbitan monostearate, polyoxyethylene (20) sorbitan tristearate, polyoxyethylene (20) sorbitan monooleate, polyoxyethylene (5) sorbitan monooleate, and polyoxyethylene (20) sorbitan trioleate, sorbitan monolaurate, sorbitan monopalmitate, sorbitan monostearate, sorbitan tristearate, sorbitan monooleate, and sorbitan trioleate.

14. The preparation according to claim 1 wherein the concentration of the one or more non-ionic surface active agent(s) is(are) about 0.01 weight percent to about 0.5 weight percent.

15. The preparation according to claim 1 wherein the aqueous immune globulin preparation is lyophilized to form a dry powder preparation.

16. An aqueous immune globulin preparation wherein the immune globulin has an increased serum half-life comprising:

about 3-8% human anti-Rh_oD immune globulin with an IgG purity of greater than 95% and a monomeric protein content of greater than 94%;

sodium chloride at about 0.25% (w/v);

very low level buffer with essentially no ionic strength;

Polysorbate 80 at about 0.01% to about 0.5% (w/v); and

L-glycine at about 0.1M.

17. A use of an immune globulin preparation according to any one of claims 1 to 16 to increase the serum half-life of an immune globulin.

18. A use of an immune globulin preparation according to any one of claims 1 to 16 to reduce the elevation of neutrophil counts.

19. A method of increasing the serum half-life of an immune globulin comprising administering an immune globulin preparation according to claims 1 to 16 to an animal in need thereof.

20. A method of reducing the elevation of neutrophil counts in a recipient of immune globulin comprising administering an immune globulin preparation according to claims 1 to 16 to an animal in need thereof.

21. A method according to claim 19 or 20 wherein said immune globulin preparation is administered intravenously.